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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/761,636	01/21/2004	Bernard Frank Bishop	PC22004B	3343

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
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GROTON, CT 06340

EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 07/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/761,636	BISHOP, BERNARD FRANK	
	Examiner	Art Unit	
	Traviss C. McIntosh	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1/21/2004
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claim 9 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 3. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Both claims limit the amount of praziquantel in claim 1 to "about" or "around" 6%.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 3-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for formulations comprising praziquantel and selamectin, does not reasonably provide enablement for formulations comprising praziquantel and any 13-monosaccharide 5-oxime avermectin. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below as seen in ***In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)***. A conclusion of lack of enablement means that, based on the evidence

regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

These factors include:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims - The nature of the invention

Claim 1 of the instant application is drawn to a formulation comprising praziquantel, a 13-monosaccharide 5-oxime avermectin, and a carrier, diluent, or adjuvant. Claims 3 and 6-9 provide various amounts of the agents. Claims 4, 10, and 11 provide various additional agents are to be included therein. And claim 5 provides the formulation is a topical or spot-on formulation.

The state of the prior art

Selamectin is known in the art to be a 13-monosaccharide 5-oxime avermectin and is known to have efficacy as an agent to control ectoparasite and helminth infections. Modifications to the structure of both avermectins and milbemycins have dramatic effect on their biological properties. For instance, the related macrocyclic lactone milbemycin oxime has a safety margin allowing use of a higher dose, which provides a broader spectrum of nematode activity. However, to date, no single avermectin or milbemycin compound has been identified with a

therapeutic ratio sufficient to allow doses of achieving efficacy in both endo- and ectoparasites in dogs and cats. It is known that subtle structural modifications to B1 avermectins produce significant alterations in potency against individual parasitic species (see Bishop et al., Veterinary Parasitology, 91, pp. 163-176, 2000, specifically the paragraph bridging pages 163-4 and page 174, first full paragraph).

The level of predictability in the art

The examiner acknowledges the probability and predictability that selamectin would be capable of being formulated with praziquantel and also have efficacy, however the art is silent with regard to the predictability of any compound being a 13-monosaccharide 5-oxime avermectin as having the capacity to be formulated with praziquantel and subsequently have efficacy, especially in view of the fact that Bishop et al. stated that subtle structural modifications to B1 avermectins are taught to produce significant alterations in potency.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to make and use the claimed formulation commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written.

The existence of working examples

All of the working examples set forth in the instant specification are directed to the use of praziquantel and selamectin. There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples

as correlative proof that any 13-monosaccharide 5-oxime avermectin would have the capacity to be formulated with praziquantel and subsequently have efficacy.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable for the making and using of a combination of praziquantel with any 13-monosaccharide 5-oxime avermectin without undue experimentation. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to prepare, characterize, and test the various 13-monosaccharide 5-oxime avermectins to determine if indeed they could be formulated with praziquantel, and then have efficacy . As set forth supra, applicants have successfully shown formulations comprising praziquantel and selamectin.

Claims 13-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of flea, heartworm, and tapeworm infections using praziquantel and selamectin, does not reasonably provide enablement for prevention of the same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The breadth of the claims - The nature of the invention

Claim 13 of the instant application is drawn to a method for preventing and treating flea, heartworm, and tapeworm infections using praziquantel and selamectin. Claims 14-17 provide various dosing regiments and claim 18 provides the method is to be practiced on a cat.

The state of the prior art

Selamectin and praziquantel are both known to have efficacy as an agent to control ectoparasite and helminth infections. However, efficacy studies in dogs and cats showed that selamectin provides therapeutic and persistent efficacy against fleas, therapeutic efficacy against gastrointestinal nematodes, and prophylactic activity against heartworms in dogs (see Bishop et al., Veterinary Parasitology, 91, pp. 163-176, 2000, specifically page 174, first paragraph). As such, prophylaxis against fleas, heartworms, and tapeworms is not recognized in the art.

The level of predictability in the art

The examiner acknowledges the probability and predictability that selamectin and praziquantel would have efficacy in treatment, however the art is silent with regard to the predictability of the formulation have preventative efficacy as asserted for fleas, heartworm, and tapeworm.

The amount of direction provided by the inventor

The instant specification is not seen to provide adequate guidance which would allow the skilled artisan to extrapolate from the disclosure and examples provided to use the claimed method commensurate in the scope with the instant claims. There is a lack of data and examples which adequately represent the scope of claim as written.

The existence of working examples

The working examples set forth in the instant specification are directed to the use of praziquantel and selamectin in various experiments. There has not been provided sufficient evidence which would warrant the skilled artisan to accept the data and information provided in the working examples as correlative proof that the formulation as set forth would have the preventative efficacy as asserted.

The quantity of experimentation needed to make and use the invention based on the content of the disclosure

Indeed, in view of the information set forth supra, the instant disclosure is not seen to be sufficient to enable for prevention of fleas, heartworm, and tapeworm. One skilled in the art could not use the entire scope of the claimed invention without undue experimentation. One skilled in the art would be confronted with an undue burden of experimentation to prepare, characterize, and test the formulation to determine if indeed the had preventative efficacy as asserted.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6 and 12-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is indefinite wherein the inclusion of parenthetical phrases leaves ambiguity and uncertainty as to whether the contents inside the parenthesis are intended as being that which

applicant intends as their invention. Clarity is respectfully requested. Removal of parentheses and replacing with commas will obviate this rejection.

Claim 12 is also indefinite for the inclusion of the parenthetical phrase "(at less than 0.1% w/v)" in line 7. It is unclear if applicants intend this as their invention or not. Removal of the parenthesis would be seen to obviate this rejection.

Claim 13 is indefinite wherein the claim is drawn to a method of "treatment **and** prophylaxis" of parasitic infections. However, it is unclear how an infection can be both treated and prevented. If a subject has had preventative therapy, then there is no need for subsequent treatment. Changing the "and" to "or" would be seen to obviate the instant rejection.

All claims which depend from an indefinite claim are also indefinite. ***Ex parte Cordova, 10 U.S.P.Q. 2d 1949, 1952 (P.T.O. Bd. App. 1989).***

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

Determining the scope and contents of the prior art.

Ascertaining the differences between the prior art and the claims at issue.
Resolving the level of ordinary skill in the pertinent art.
Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-12 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey (WO 98/06407) in view of Lukas et al. (US 2002/0028780).

Claim 1 is drawn to a formulation comprising a 13-monosaccharide 5-oxime avermectin at about 1-16% w/v and praziquantel at about 0.5-10% w/v, together with a carrier, diluent, or adjuvant. It is noted that these claims are being read wherein the avermectin derivative is selamectin, as the examiner believes that is all applicants have support for, as set forth supra. Claim 2 provides the avermectin is selamectin. Claim 8 provides praziquantel is present at about 3-9% w/v, and claims 3 and 9 provide praziquantel is present at about 6%. Claim 4 provides there is also a ether and optionally a solvent. Claim 5 provides the formulation is for topical or spot-on application. Claims 6 provides selamectin is provided at around 6-12 mg/kg and praziquantel at up to 18 mg/kg. Claim 7 provides the selamectin is present at about 6-12% w/v. Claim 10 provides that DEGMME or DPGMME is present. Claim 11 provides that a solvent of either ethanol or isopropanol is present. Claim 12 provides for a specific formulation. And claim 19 is drawn to a kit comprising selamectin and praziquantel and a carrier. It is noted that the written instructions of claim 19 are of no patentable import to the claim.

Harvey teaches of a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from avermectins and milbemycins, a suitable organic solvent and a carrier. The praziquantel is taught to be present in an amount ranging from 1-10% w/v (see page 2, lines 20-21). Harvey also teaches praziquantel can be combined with any compound of the avermectin group to achieve the

purpose of their invention (page 19, lines 19-20). What is not taught is to specifically combine selamectin with praziquantel.

Lukas et al. teach an antiparasitic formulation comprising 0.1-50% w/v of an avermectin or milbemycin having endo- or ectoparasitic activity, 1-50% w/v of an ether, optionally an antioxidant, and a solvent (see page 1, column 1). Lukas et al. disclose that the preferred avermectin in their formulation is selamectin and the preferred ether is DEGMME or DPGMME (see page 1, column 2). Additionally, Lukas et al. teach that the preferred solvent is ethanol or isopropanol (page 2, column 1). Lukas et al. also teach that the antioxidant present can be BHT at a level of less than 0.2% w/v. Lukas et al. teach that their formulations can be prepared for topical or spot-on use, and administered to a dog or cat (page 1, column 2- page 2, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the active agents, selamectin and praziquantel, to form a single composition with these references before them. One would have been motivated to combine praziquantel and selamectin in a formulation in the claimed amounts because the agents individually are know to be effective in those amounts. Moreover, one would have been motivated to combine the active agents because it is obvious to combine two compositions each of which is used for the same purpose, to form a new composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. ***In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).*** (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also ***In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960)*** (Claims directed to a method and material for treating cast iron using a mixture

comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and ***Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992)*** (mixture of two known herbicides held prima facie obvious). In the instant case, Harvey teaches it is advantageous to combine two or more anthelmintics with different activity in one composition to obtain a composition having a broad spectrum of activity, and thus reduce the time spent treating the animal and thus reducing the stress on the animal. One would have been motivated to combine these agents to form a new composition which would be used for the very same purpose.

Claims 13-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harvey (WO 98/06407) in view of Lukas et al. (US 2002/0028780).

Claim 13 is drawn to a method of treating a flea, heartworm, or tapeworm infection in a mammal by administering a formulation comprising selamectin and praziquantel. Claims 14-18 provide the agents are administered together, separately, via the same route, via different routes, and to a cat.

Harvey teaches methods of treating parasitic infections of flea, heartworm, or tapeworm by administering a veterinary composition containing an effective amount of praziquantel, an effective amount of at least one macrolide anthelmintic selected from avermectins and milbemycins, a suitable organic solvent and a carrier. The praziquantel is taught to be present in an amount ranging from 1-10% w/v (see page 2, lines 20-21). Harvey also teaches praziquantel can be combined with any compound of the avermectin group to achieve the purpose of their

invention (page 19, lines 19-20). What is not taught is methods using the specific combination of selamectin with praziquantel.

Lukas et al. teach of methods of treating endo- and ectoparasitic infections by using an antiparasitic formulation comprising 0.1-50% w/v of an avermectin or milbemycin having endo- or ectoparasitic activity, 1-50% w/v of an ether, optionally an antioxidant, and a solvent (see page 1, column 1). Lukas et al. disclose that the preferred avermectin in their formulation is selamectin and the preferred ether is DEGMME or DPGMME (see page 1, column 2). Additionally, Lukas et al. teach that the preferred solvent is ethanol or isopropanol (page 2, column 1). Lukas et al. also teach that the antioxidant present can be BHT at a level of less than 0.2% w/v. Lukas et al. teach that their formulations can be prepared for topical or spot-on use, and administered to a dog or cat (page 1, column 2- page 2, column 1).

It would have been obvious to one of ordinary skill in the art at the time of the invention to combine the active agents, selamectin and praziquantel, to form a single composition and treat endo- or ectoparasites with these references before them. One would have been motivated to combine praziquantel and selamectin in a formulation in the claimed amounts because the agents individually are know to be effective in those amounts. Moreover, one would have been motivated to combine the active agents because it is obvious to combine two compositions each of which is used for the same purpose, to form a new composition that is to be used for the very same purpose. The idea of combining them flows logically from their having been individually taught in the prior art. ***In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).*** (Claims to a process of preparing a spray-dried detergent by mixing together two conventional spray-dried detergents were held to be prima facie obvious.). See also ***In re***

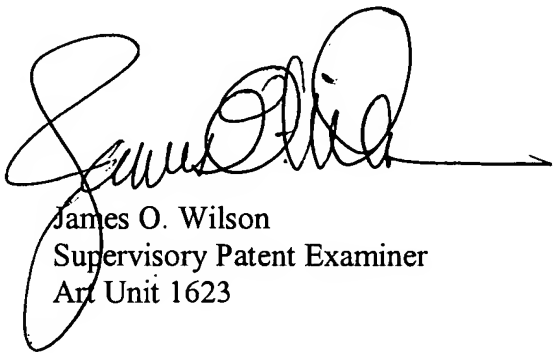
Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Claims directed to a method and material for treating cast iron using a mixture comprising calcium carbide and magnesium oxide were held unpatentable over prior art disclosures that the aforementioned components individually promote the formation of a nodular structure in cast iron.); and ***Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992)*** (mixture of two known herbicides held prima facie obvious). In the instant case, Harvey teaches it is advantageous to combine two or more anthelmintics with different activity in one composition to obtain a composition having a broad spectrum of activity, and thus reduce the time spent treating the animal and thus reducing the stress on the animal. One would have been motivated to combine these agents to form a new composition which would be used for the very same purpose.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



James O. Wilson
Supervisory Patent Examiner
Art Unit 1623

Traviss C. McIntosh
June 25, 2005